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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,193	MIYAZAWA ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-13 and 71-75* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,3-14,16,17,22,26,29,31,35,38-40,44,45,47,48,50-54,57-59,61-65,67,68 and 70-91.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,16,17,22,26,29,31,35,38-40,44,45,47,48,50-54,57-59,61-65,67,68 and 70.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed on 17 September 2009. Claims 2, 15, 18-21, 23-25, 27, 28, 30, 32-34, 36, 37, 41-43, 46, 49, 55, 56, 60, 66, 69, have been cancelled. Claims 71-91 have been added. Claims 1, 3-14, 16, 17, 22, 26, 29, 31, 35, 38-40, 44, 45, 47, 48, 50-54, 57-59, 61-65, 67, 68 and 70-91 are pending.

Election/Restriction

Applicant's election with traverse of Group I (claims 1, 3-13 and 71-75) and the microsatellite loci species of D22S272, in the reply filed on 17 September 2009, is acknowledged.

The traversal of the Group election is on the grounds that the various invention groups represent different embodiments of a "single, searchable, unifying aspect based on the discovery that DNA sequences on certain loci, all on chromosome 22, confer a resistance to infection, especially viral resistance as exemplified by HIV resistance". However, the instant claims do not recite the same general inventive concept as asserted by the Applicant. The "single, searchable, unifying aspect" of using DNA sequence on chromosome 22 to identify resistance to infection is only recited in the elected claims 1, 3-13 and 71-75 but not in the remaining claims, as already set forth on page 2-4 in the previous Office Action mailed 17 March 2009. Thus, the asserted "single, searchable, unifying aspect" is not the "shared technical feature" for all of the instant claims.

The traversal of the sequence election is on the grounds that Applicants cannot be limited to a single primer sequence. However, this argument only applies to the elected claims 13 and 75, but not to the non-elected claim 38, which is drawn to a vaccine.

Applicant further traverse on the ground that it would not be unreasonable or burdensome to examine all the species. This is not found persuasive because applicants have not argued with particularity the basis for the requirement for restriction, but have merely asserted that the subject matter overlaps and that no burden of search is involved. Applicants do not indicate how any sequence mentioned in the claims is related to or "overlaps" any other sequence mentioned in the claims, nor does applicant indicate how any of the major groups outlined in the requirement for restriction overlap. Finally, overlap of subject matter does not automatically translate into coextensive searches that are not a burden on the USPTO. The searches of microsatellite species are not coextensive and each requires its own search and considerations of other patentability issues.

Claims 4, 16, 17, 22, 26, 29, 31, 35, 38-40, 44, 45, 47, 48, 50-54, 57-59, 61-65, 67, 68 and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species/sequence. Upon further consideration of the claimed invention as recited in claims 1, 3-13, and 71-75, the primer pair sequences of SEQ ID NO:3 and SEQ ID NO:4 are examined together.

Claims 1, 3-13, and 71-75 are examined to the extent that they read on the elected species and sequence.

In order to facilitate the prosecution of this application, Applicant is requested to consider inserting a claim drawn solely to the above elected species and sequence and canceling all non-elected embodiments from the claims.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. §119(a)-(d), which papers have been entered. Applicant's provision of foreign priority documents, United Kindgom 0223982.0, is acknowledged. Therefore, the priority date is deemed to be the filing date of the priority application, 16 October 2002.

Information Disclosure Statement

Applicant's Information Disclosure Statements (IDS) filed 13 April 2005 (four pages total) has been received and entered into the application. As reflected by the attached, completed copies of form PTO-1449A, the Examiner has considered the cited references.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See pages 14 and 24, for example.

Appropriate correction is required.

Claim Objections

Claim 1 is objected to because of the grammatical error in the phrase "to identify the alleles present at least one of the microsatellite loci" and the list missing the word "D33S1169" preceding the wherein clause.

Appropriate correction is required.

Double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-7 and 71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 50-54 and 61-63 of copending Application No. 11/793575. Although the conflicting claims are not

identical, they are not patentably distinct from each other because the instant claims 1, 3-7 and 71 are generic to all that are recited in the copending claims 50-54 and 61-63. That is, claims 50-54 and 61-63 of copending Application No. 11/793575 fall entirely within the scope of the instant claims 1, 3-7 and 71 or, in other words, claims 1, 3-7 and 71 are anticipated by claims 50-54 and 61-63 of copending Application No. 11/793575. Specifically, the method of determining resistance to infection comprising using a microsatellite loci of at least D22S929, D22S277, D22S264, D22S423, D22S418, D22S272, or D22S1169 as recited in the instant claim 1 is the same method of determining resistance to infection comprising using a nucleic acid sequence encoding a gene located in the region of human chromosome 22 between the loci D22S277 and D22S423 or a functional fragment thereof.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 71 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 71 recites "a nucleic acid sequence present between microsattelite loci D22S929 and D22S1169," which is vague and indefinite because the phrase can be

interpreted as the entire length of sequence between microsattelite loci D22S929 and D22S1169 or any portion thereof. Furthermore, the precise nucleic acid sequence between microsattelite loci D22S929 and D22S1169 is not readily apparent. While the name of the microsatellite loci itself may have some notion of location of the nucleotide sequence on the human chromosome, there is nothing in the claims that distinctly describes the exact sequence of the nucleic acid. Therefore, it is not clear from the limitations in the claim what is intended to be the metes and bounds of the claimed invention.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, 1st ¶

Written Description Rejection

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-13 and 71-75 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings or structural chemical formulas, or by disclosure of relevant, identifying characteristics, *i.e.*, complete/partial structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, by predictability in the art, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Claims 1, 3-13 and 71-75 are drawn to a method of determining resistance to infection comprising identifying alleles present at the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169. Claim 3, 13, 71 and 75 is also drawn to identifying presence of a nucleic acid sequence, complementary nucleic acids or fragments, homologues, splice variants, polymorphisms, or derivatives of microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169. The claims do not limit the size or the sequence structure of the allele, variant, homologue, complement, and derivative. Thus, the instant claims recite a broad genus of highly variable nucleic acid sequences.

In *Regents of the University of California v. Eli Lilly and Co.* 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), the Court decided that adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." *Id.* 43 USPQ2d at 1404 (quoting *Fiers*, 984 F.2d at 1171, 25

USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice, Id.

The cited case law is relevant to the instant invention because there is limited disclosure of the structure, formula, or physical properties of an "allele, homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" and there is only a disclosure of the functional characteristic of the "allele, homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" as a genetic marker for infection resistance, rather than of what it is.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus. *Regents of the University of California v. Eli Lilly& Co.*, 199 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly & Co.*, the court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. A "representative number of species" means that the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP §2163 II.A.3a.ii. Although the M.P.E.P. does not define what constitutes

a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a genus of nucleic acids that is defined only by the function as a genetic marker for resistance to infection. The claims encompass an inordinate number of species with disparate functional activities that are neither described nor contemplated by Applicants. The genus of an "allele, homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" of microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169 is not adequately described because the specification provides description for homology between mouse chromosome 15 containing Rfv3 and human chromosome 22 and the detection of various size fragments, ranging from 126bp to 221bp, using the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and D22S1169 in HIV-expose un-infected subjects (see Table 4 on page 38). However, the specification does not identify any partial structural features or motifs that correspond to the functional limitation of resistance to infection.

The specification does not disclose a representative number of species of "allele, homologue, splice variant, polymorphism, derivative, complementary nucleic acid or fragment" of microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 and/or D22S1169, relative to the size of the claimed genera. As a result, one

of skill in the art could not conclude that Applicant was in possession of the claimed methods at the time of the invention. Therefore, claims 1, 3-13 and 71-75 do not meet the written description provision of 35 U.S.C. §112, first paragraph.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever* is now *claimed*." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC §112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

Claim Rejections - 35 USC § 112, 1st ¶

Scope of Enablement Rejection

Claims 1, 3-13 and 71-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for determining resistance to HIV infection comprising sequencing for APOBEC3 gene-coding alleles at the claimed microsatellite markers, does not reasonably provide enablement for determining resistance to any other infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

Nature of the invention. The claims are drawn to a method of determining a resistance to infection comprising assay a DNA bearing sample from a subject to detect allele presence with at least one of the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169.

Breadth of the claims. The breadth of the claimed invention is exceedingly large and fails to receive adequate support in the specification. The broad claims encompass determining resistance of *all infectious diseases* in *any animal* with *any size fragment* of alleles at the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. Claim 3 further encompasses homologues, splice variants or derivatives of the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. The instant claimed microsatellite allele/nucleic acid sequence/ homologues, splice variants or derivatives

are not limited to a single nucleic acid sequence, encompassing use of a wide variety of sequences encoding uncharacterized proteins.

Working examples. The disclosure fails to provide any working embodiments that meet the claimed limitations. There is an example showing in mice linkage between Friend leukemia virus-neutralizing antibody titer and single-stranded length polymorphism (SSLP) analysis of genotypes at the mouse chromosome 15 locus of the *Rfv-3* gene, the mouse gene that confers resistance to Friend's virus infection (see page 19-21 and 23-25, paragraph [0072]-[0074], [0076], and [0078]-[0082]). There is another example showing SSLP genotype analysis of HIV-exposed but serum-negative/un-infected human subjects with human microsatellite markers that are syntenic with the mouse microsatellite markers (see page 20-22 and 25-27, paragraph [0075], [0077], [0083]-[0085]). However, no other working examples are present to show a correlation between the presence of alleles at the microsatellite marker, D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169, and the resistance to any other type of infection.

Guidance in the specification. The disclosure fails to provide sufficient guidance pertaining to the correlation between the genotypic presence of alleles at the claimed microsatellite loci and phenotype of resistance to infection. Even though the working example teaches the DNA sequence homology between mouse chromosome 15, which contains the Friend's virus-resistance gene Rfv3, and the human chromosome 22 (see Figures 2, 4 and 5), the specification is limited to the association of HIV-exposed un-infected phenotype with the genotype of allele frequency at only

some of the chromosome 22 locus (see Figure 6 or Table 4 on page 38). Actually, the specification does not even show that every claimed microsatellite loci has an allele frequency correlated with the resistance to HIV infection. As set forth by the data in Table 4 on page 38, only the D22S272 and D22S423 microsatellite markers show significant differences between the HIV-exposed un-infected group and the infected or the healthy control group. The specification only states that alleles at D22S929, D22S2272, D22S284 and D22S1166 are more frequent in uninfected HIV-exposed patients (see page 39).

Furthermore, the specification does not provide evidence establishing that the resistance to HIV infection can be extrapolated to resistance to all kinds of infection. The specification only discloses Applicant's hypotheses that the IgA antibodies in HIV-exposed un-infected people provide the immune response against all types of infection and that the IgA antibody-producing individuals can be determined by genotyping with the chromosome 22 microsatellite markers, which is based on the observation of high titers of IgA antibodies in the serum of subjects that possess the alleles at the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. However, without sufficient guidance pertaining to resistance to infection, the skilled artisan has only been extended an undue invitation to further experimentation to ascertain which type of infection is associated with the presence of alleles at which of the microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169.

State of the prior art and Predictability. At the time the invention was made, a method of determining resistance to infection by genotyping the microsatellite loci in humans is not considered routine in the art. The prior art only shows that microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 are effective for genotype analysis of an identified gene that is associated with a resistance to a specific type of infection, such as the HIV-inhibiting APOBEC3 (see Sheehy *et al.*), identified by Jarmuz *et al.* on human chromosome 22, which is shown by Super *et al.* to share sequence homology with mouse chromosome 15 containing the Friend's virus resistance gene, *Rfv3*. The prior art fails to provide sufficient illumination pertaining to the correlation between a resistance to any infection and the presence of any alleles at the instantly claimed microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. However, the prior art discloses an association of cancer or tumor genes with chromosome 22 microsatellite markers D22S423, D22S272, and D22S277 (see Ingvarsson *et al.*), a linkage of the manifestation of schizophrenic symptoms to polymorphism near the microsatellite marker D22S264 (see Takase *et al.*), and a correspondence of Der(22) syndrome and Velo-Cardio-Facial Syndrome/DiGeorge Syndrome with the presence of alleles at marker D22S264 (see Funke *et al.*). In conclusion, the phenotypic or clinical manifestation of the mere presence of alleles at microsatellite loci, at D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 is rather unpredictable. The genotypic result of these alleles, complementary nucleic acid, variant, homologue, or derivative alone is uninformative without detecting a specific

gene that is correlated with infection resistance and without any phenotypic assays confirming the individual's resistance to a specific source of infection. In other words, the prior art only teaches that the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169 is effective for genotype analysis of an identified gene that is associated with a specific disease condition.

Furthermore, it is known for proteins that even a single amino acid mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the recitation of "homologues, splice variants, or derivatives of the microsatellite loci" results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated function of resistance to infection and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit certain specific sequences may be conserved over biomolecules of related function upon a significant amount of further research. See Pakula *et al.* (1989) and Oestreicher *et al.* (1995) for example.

Amount of experimentation necessary. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See *Fields v. Conover*, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). In the instant case, [a pharmaceutical HIV-vaccine comprising recombinant adenovirus particles] is not considered routine in the art and, without sufficient guidance to elicit therapeutic effects,

the experimentation left to those skilled in the art is undue or unreasonable under the circumstances.

It is not obvious from the disclosure how one can determine resistance to all infection with the microsatellite marker D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169. M.P.E.P. §2164.03 [R-2] states: [I]n applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soil*, 97 F.2d 623,624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488,496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991).

Applicants have not provided sufficient guidance to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success and without undue experimentation. In the absence of such guidance and evidence, the specification fails to provide an enabling disclosure. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. For the reasons discussed above, it would require undue and unpredictable experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-12 and 71-74 are rejected under 35 U.S.C. §103(a) as being unpatentable over Stephens *et al.* (1998) in view of Super *et al.* (1999), Jarmuz *et al.* (2002 July 14) and Sheehy *et al.* (2002 August 8).

The instant claims are directed to a method comprising assaying a DNA sample from a subject to identify the presence of at least one of the microsatellite loci D22S929, D22S277, D22S264, D22S423, D22S418, D22S272 or D22S1169, which is from human chromosome 22 and indicative of resistance to infection.

Stephens *et al.* discloses a method comprising chromosomal haplotype analysis of study subject samples to identify the presence of microsatellite loci from human chromosome 3p21 region containing the CCR gene complex to detect the CCR5-delta32 AIDS-resistance allele. See page 1508-1509, Methods.

Stephens *et al.* does not disclose any microsatellite loci from human chromosome 22.

Super *et al.* discloses that the human chromosome 22q has homology with mouse chromosome 15, where the Friend Retrovirus Resistance Gene, *Rfv3*, is located. Super *et al.* also suggests further mapping of the human chromosome 22q region may uncover additional candidate genes that can serve as microsatellite markers for the

retrovirus resistance gene in humans. See page 7850, right column, second paragraph, and page 7851, Figure 3B.

Jarmuz *et al.* discloses that APOBEC3 is located on human chromosome 22. See page 286, right column.

Sheehy *et al.* discloses that CEM15, which is the synonym for APOBEC3, inhibits the infectivity of HIV virions lacking the Vif protein. See page 649, the paragraph connecting the two columns. This means that the CEM15 or APOBEC3 gene confers resistance to HIV infection.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Stephens *et al.* so as to include more microsatellite loci from human chromosome 22, as suggested by Super *et al.*, containing retrovirus-resistant genes like the HIV-inhibiting APOBEC3, as suggested by Sheehy *et al.* and Jarmuz *et al.* One having ordinary skill in the art would have been motivated to make such a modification to optimize the method to more effectively detect all genes that confer resistance to HIV infection. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 13 and 75 are rejected under 35 U.S.C. §103(a) as being unpatentable over Stephens *et al.* (1998) in view of Super *et al.* (1999), Jarmuz *et al.* (2002 July 14), Sheehy *et al.* (2002 August 8), and Ingvarsson *et al.* (2002 March 20).

The instant invention is further limited to the PCR primers for amplification of the microsatellite marker D22S272.

The disclosure of Stephens *et al.*, Super *et al.*, Jarmuz *et al.*, and Sheehy *et al.* is set forth above. None of the references specifically teach the PCR primers of the microsatellite marker D22S272.

Ingvarsson *et al.* discloses analyzing with single-strand polymorphism and sequencing DNA from subject samples using PCR primers that amplify seven microsatellite markers, D22S277, D22S283, D22S1177, D22S272, D22S423, D22S1179 and D22S282 to detect genes at chromosome 22q. See the second page, Materials and Methods.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Stephens *et al.* so as to add the PCR primers for microsatellite loci from human chromosome 22, as suggested by Ingvarsson *et al.* One having ordinary skill in the art would have been motivated to make such a modification to optimize the method to more effectively detect all genes that confer resistance to HIV infection. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the application as filed so as not to add new matter. See MPEP §714.02 and §2163.06.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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28 September 2009